DETAILED ACTION

Response to Amendment

The amendment filed on February 3, 2011 has been acknowledged. Claims 14, 15, 18-20, 23-31, 34-37, 39 and 40 remain pending. Applicant amended claims 14 and 34.

Despite the amendment, the rejections are maintained.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims **14, 15, 18-20, 23-26, 28-31, 34-37, 39 and 40** are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Dam et al. (US 2003/0008411 A1) in view of Quake et al. (US 2002/0037499 A1).

Van Dam et al. disclose a microfluidic device and a method for synthesizing a library of compounds by using the microfluidic device (see claim 15), which includes DNA synthesis (see [0056]). The device comprises a solid substrate layer and an elastomeric layer attached to the solid substrate wherein the surface of the solid substrate is immobilized with ligands for binding analytes of interest. The device further comprises a plurality of control channels associated with each of the first and second flow channels. Each control channel comprises a chamber delimited by an elastic membrane. Upon the application of an actuation force within a control channel, the elastic membrane of the control channel deflects into the flow channel to block fluid flow through the flow channel. The control channels also act as a pump when they are

actuated sequentially to facilitate the flow of fluids through the flow channels (see [0068] and [0069]).

The method disclosed by the reference comprises the steps of:

- providing the device described above,
- manipulating the control valves to restrict flow in the second flow channels,
- introducing a solution comprising ligands into the first flow channels to attach the ligands to the surface of the first flow channels,
- removing the restriction in the second flow channels and manipulating the control valves to restrict flow in the first flow channels,
- introducing a reagent into the first flow channels such that the reagent binds to the ligands immobilized to the surface of the solid substrate,
- introducing a sample solution into the second flow channels such that the sample in the sample solution circulates through the flow channels and binds the reagents bound to the immobilized ligands (see claims 25 and 26), and
- detecting the binding reaction (see [0122]).

While Van Dam et al. disclose that the valves at the inlet and the outlet of the device can be manipulated to redirect the flow of liquid in a serpentine manner (see [0190]), Van Dam et al. do not disclose the step of manipulating the valves to form a closed loop as recited in the claims.

Quake et al. disclose a microfluidic device similar to the device disclosed by Van Dam et al. Like the device disclosed by Van Dam et al., the device comprises intersecting microfluidic channels and elastomeric valves. Quake et al. also disclose a

method for detecting analytes, the method comprising the steps of hybridizing a sample with probes immobilized to the surface of the microfluidic channels. Quake et al. also disclose the step of manipulating the valves to form a closed loop of flow channels. The closed loop enables the sample to circulate throughout the loop and properly hybridize with the probes (see Abstract and [0076]). The loop can be formed by actuating independently controlled elastomeric valves that can also act as a pump (see [0079]). In light of the disclosure of Quake et al., it would have been obvious to one of ordinary skill in the art to provide the device disclosed by Van Dam et al. with independently controlled loop-forming elastomeric valves, and manipulate said valves to form closed looped channels and pump fluids during the hybridization step to ensure that the sample and the reagents properly hybridize. Naturally, if one were to form a closed loop of flow channels within the Van Dam et al. device, the closed loop would span multiple rows and columns of channels.

With respect to claim 15, Van Dam et al. disclose that ligands that have not attached to the surface of the flow channels are washed using a solvent prior to the sample being introduced into the flow channels (see [0084]).

With respect to claims 18 and 35, Van Dam et al. disclose that the surfaces of the substrate layer and the elastomeric layer can comprise grooves/wells that define a plurality of first flow channels intersecting a plurality of second flow channels (see claim 24 and [0048]).

With respect to claims 19, 20 and 39, the control channels act as a pump when they are sequentially actuated, as discussed above.

With respect to claims 23-26, 36 and 37, Van Dam et al. disclose the step of derivatizing the solid substrate and determining the efficacy of the derivatization after detaching the elastomeric layer from the substrate layer (see [0122]). This is accomplished by reacting the immobilized ligands with fluorophores and detecting the fluorescence. In light of the disclosure, it would have been obvious to one of ordinary skill in the art to tag the synthesized compounds produced by the method described above and detect the fluorescence using a fluorescent microscope in order to observe the efficacy of the synthesis.

With respect to claims 28 and 30, Van Dam et al. disclose that the term "reagent" involved in the assay refers to oligonucleotides, peptides, monomers, and other small molecules that are building blocks of a larger molecule (see [0056]).

With respect to claim 29, Van Dam et al. disclose that the device can be used to study mutations, gene regulation and gene expression, which are within the scope of "cell proliferation" recited in the claims.

With respect to claim 31, given that the device disclosed by Van Dam et al. is adapted to perform binding assays, it would have been obvious to one of ordinary skill in the art to react any two entities that bind using the device disclosed by Van Dam et al., including a cell as the reagent and antimicrobes as the sample in order to observe the effects of the antimicrobes on the cell.

With respect to claim 40, Quake et al. disclose the use of a control channel disposed within an elastomeric layer as a loop forming control valve, as discussed above.

Claim **27** is rejected under 35 U.S.C. 103(a) as being unpatentable over Van Dam et al. in view of Quake et al. as applied to claims 14, 15, 18-20, 23-26, 28-31, 34-37, 39 and 40, and further in view of Raillard et al. (US 2002/0102577 A1).

Neither Van Dam et al. nor Quake et al. disclose the usage of a non-optical detector to observe the compound synthesis.

Raillard et al. disclose a method for labeling probes with radio-isotopes that emit radiation (see [0132]). The probe is detected using a detector that is sensitive to radiation.

In light of the disclosure of Raillard et al., it would have been obvious to one of ordinary skill in the art to tag the synthesized compounds produced by the modified Van Dam et al. method with radio-isotope probes instead of fluorophores and detect the radiation using a radiation detector in order to observe the efficacy of the synthesis in the event that fluorophores are not available.

Response to Arguments

Applicant's arguments with respect to the claims have been fully considered but they are not persuasive.

Applicant argues that the claims are patentably distinct from the disclosure of Van Dam et al. and Quake et al. because neither reference disclose the limitation "wherein the first valve of the set of loop forming control valves comprises a control channel of the pump". This argument is not persuasive. As indicated above in the rejection, Quake et al. disclose the use of independently actuated control channels that

can be pressurized to form closed loop channels within its device, wherein the control channels can also be sequentially actuated to pump fluid through the closed loop channels (see [0079]). Because Quake et al. disclose the feature "wherein the first valve of the set of loop forming control valves comprises a control channel of the pump", the rejections are maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL S. HYUN whose telephone number is (571)272-8559. The examiner can normally be reached on Monday-Friday 10AM-6:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, In Suk Bullock can be reached on (571)-272-5954. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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